survival rate of patients. The initial chemotherapy regimen for ovarian cancer includes the combination of carboplatin (Paraplatin) and paclitaxel (taxol). Years of clinical trials have proved this combination to be most effective after effective surgery—reduces tumor volume in about 80% of the women with newly diagnosed ovarian cancer and 40% to 50% will have complete regression—but studies continue to look for ways to improve patient response. Recent abdominal infusion of chemotherapeutics to target hard-to-reach cells in combination with intravenous delivery has increased the effectiveness. However, severe side effects often lead to an incomplete course of treatment. Some other chemotherapeutic agents include doxorubicin, cisplatin, cyclophosphamide, bleomycin, etoposide, vinblastine, topotecan hydrochloride, ifosfamide, 5-fluorouracil and melphalan. More recently, clinical trials have demonstrated that intraperitoneal administration of cisplatin confers a survival advantage compared to systemic intravenous chemotherapy (Cannistra and McGuire, 2007). The excellent survival rates for women with early stage disease receiving chemotherapy provide a strong rationale for research efforts to develop strategies to improve the detection of ovarian cancer. Furthermore, the discovery of new ovarian cancer-related biomarkers will lead to the development of more effective therapeutic strategies with minimal side effects for the future treatment of ovarian cancer.

**[0008]** Notwithstanding these recent advances in the understanding and the treatment for ovarian cancer, the use of chemotherapy is invariably associated with severe adverse reactions, which limit their use. Consequently, the need for more specific strategies such as combining antigen tissue specificity with the selectivity of monoclonal antibodies should permit a significant reduction in off-target-associated side effects. The use of monoclonal antibodies for the therapy of ovarian cancer is beginning to emerge with an increasing number of ongoing clinical trials (Oei et al., 2008; Nicodemus and berek, 2005). Most of these trials have examined the use of monoclonal antibodies conjugated to radioisotopes, such as yttrium-90, or antibodies that target tumor antigens already identified in other cancer types. An example of this is the use of bevacizumab, which targets vascular endothelial growth factor (Burger, 2007). There are very few ovarian cancer specific antigens that are currently under investigation as therapeutic targets for monoclonal antibodies. Some examples include the use of a protein termed B7-H4 (Simon et al., 2006) and more recently folate receptor-alpha (Ebel et al., 2007), the latter of which has recently entered Phase II clinical trials.

**[0009]** Kidney associated antigen 1 (KAAG1) was originally cloned from a cDNA library derived from a histocompatibility leukocyte antigen-B7 renal carcinoma cell line as an antigenic peptide presented to cytotoxic T lymphocytes (Van den Eynde et al., 1999; Genebank accession no. Q9UBP8, SEQ ID NOs.:28; 29). The locus containing KAAG1 was found to encode two genes transcribed on opposite DNA strands. The sense strand was found to encode a transcript that encodes a protein termed DCDC2. Expression studies by these authors found that the KAAG1 antisense transcript was tumor specific and exhibited very little expression in normal tissues whereas the DCDC2 sense transcript was ubiquitously expressed (Van den Eynde et al., 1999). The expression of the KAAG1 transcript in cancer, and in particular ovarian cancer, renal cancer, lung cancer, colon cancer, breast cancer and melanoma was disclosed in the published patent application No. PCT/CA2007/001134 (the entire content of which is incorporated herein by reference). Van den Eynde et al., also observed RNA expression in renal carcinomas, colorectal carcinomas, melanomas, sarcomas, leukemias, brain tumors, thyroid tumors, mammary carcinomas, prostatic carcinomas, oesophageal carcinomas, bladder tumor, lung carcinomas and head and neck tumors. Recently, strong genetic evidence obtained through linkage disequilibrium studies found that the VMP/DCDC2/KAAG1 locus was associated with dyslexia (Schumacher et al., 2006; Cope et al., 2005). One of these reports pointed to the DCDC2 marker as the culprit in dyslexic patients since the function of this protein in cortical neuron migration was in accordance with symptoms of these patients who often display abnormal neuronal migration and maturation (Schumacher et al., 2006).

## SUMMARY OF THE INVENTION

**[0010]** The invention relates to specific anti-KAAG1 antibodies and antigen binding fragments and their use for the treatment, detection and diagnosis of cancer comprising tumor cells expressing KAAG1 or a KAAG1 variant. Exemplary embodiments of such cancer includes, for example, ovarian cancer, skin cancer, renal cancer, colorectal cancer, sarcoma, leukemia, brain cancer, cancer of the thyroid, breast cancer, prostate cancer, cancer of the oesophagus, bladder cancer, lung cancer and head and neck cancer.

**[0011]** The antibodies or antigen binding fragments may be particularly effective at targeting KAAG1 or KAAG1 variant expressed at the surface of the tumor cells.

**[0012]** In fact, the antibodies and antigen binding fragments of the present invention appear to have improved ability to bind to KAAG1-expressing tumor cells in comparison with, for example, the 3D3 and 3G10 antibodies disclosed in PCT/CA2009/001586 (the entire content of which is incorporated herein by reference). These antibodies and antigen binding fragments are also internalized and may therefore be useful to deliver therapeutic agents to tumor cells. Our results suggest that antibodies and antigen binding fragments having the desired characteristics (e.g., improved binding and internalization) generally bind to a C-terminal region of KAAG1 delimited by amino acids 61 to 84. However, although both the 3A4 and 3G10 antibodies bind to the same region, the 3A4 antibody appears to bind to the surface of tumor cells more efficiently than the 3G10 antibody. In particular, cancer cells that express the KAAG1 antigen require approximately 10-fold less 3A4 compared to 3G10 in flow cytometry experiments, an approach that measures the direct binding of the antibodies to the surface of the cells. In addition, in binding experiments using surface plasmon resonance, it was discovered that the affinity of 3A4 for KAAG1 is below 10 picomolar, whereas antibodies 3D3 and 3G10 exhibited affinities greater than 200 nanomolar (20-fold lower affinity). Therefore, these increases in binding ability of 3A4 are expected to translate into improved therapeutic activity.

**[0013]** The present invention provides in one aspect thereof, an isolated or substantially purified antibody or antigen binding fragment which may be capable of specific binding to a sequence which is identical to at least 10 (e.g., 10 to 20 or more) consecutive amino acids located between amino acids 61 to 84 of KAAG1 (SEQ ID NO.:29)